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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,472	10/04/2005	Masashi Ito	082368-001500US	8056

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TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
ART UNIT	**PAPER NUMBER**
1633	

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06/16/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,472	ITO ET AL.	
	Examiner	Art Unit	
	FEREYDOUN G. SAJJADI	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 17-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 17-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/14/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Request for Continued Examination

A request for continued examination under 37 CFR §1.114, including the fee set forth in 37 CFR §1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR §1.114, and the fee set forth in 37 CFR §1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR §1.114. Applicant's submission filed on March 31, 2009 that includes a response to the office Action dated October 2, 2008, has been entered. Claim 6 has been amended. No claims were cancelled or newly added. The claims have been examined commensurate in scope with the elected species of insulin genes as the foreign DNA encoding a secreted protein.

Claims 1-11 and 17-19 are pending in the Application and under current examination.

Information Disclosure Statement

Document F1 submitted in compliance with 37 CFR §1.97(g),(h), and 37 CFR §1.98(a)(2) has been considered by the Examiner and indicated as such on Supplemental Form SB/08.

Response to Claim Objection

Claim 6 was objected to for minor informalities regarding the isolation of preadipocytes, in the previous office action dated October 2, 2008. In view of Applicants' claim amendment limiting the language to preadipocytes and obviating the ground for objection, the previous objection is hereby withdrawn.

New Claim Rejections - 35 USC § 112- Second Paragraph

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is unclear in several respects. The claim is directed to a preadipocyte population with ability to significantly express a secreted protein *in vivo* for at least 20 days. It is unclear what degree of expression is considered significant. The claim is further unclear in its recitation of expression for at least 20 days, setting no upper limit for the number of days the protein is expressed. The claim is yet further unclear, because the "at least 20 days" additionally suggests that the preadipocyte population has an infinite lifespan *in vivo*. Thus, the metes and bounds of the claim remain undefined.

Withdrawn Claim Rejections - 35 USC § 102

Claim 1-5, 8-9, 17 and 18 were rejected under 35 U.S.C. §102(e) as being anticipated by Furcht et al. (U.S. Patent No. 7,015,037, Priority to Aug. 5, 1999), in the previous office Action dated October 2, 2008. Applicants have supplied a Declaration under 37 C.F.R. § 1.132 by Mr. Masayuki Aso, providing experimental data demonstrating that the claimed primary cultured preadipocytes are distinct from the multipotent adult stem cells MASCs of Furcht et al., by expressing cell surface markers CD44, Muc18(CD146) and CD36 on the preadipocyte cell surface. It should be noted however, that as disclosed by Applicants' specification, preadipocytes normally exist as stromal cells that have not yet differentiated (pp. 4-5, bridging), and thus the claimed preadipocytes may represent intermediates between the MASCs and mature adipocytes described by Furcht et al. However, because such cannot be definitively established due to

potential de-differentiation during ceiling culture, the rejection is hereby withdrawn. Applicants' arguments are moot in view of the withdrawn rejection.

Withdrawn Claim Rejections - 35 USC § 103

Claims 9-11 were rejected under 35 U.S.C. §103(a) as being unpatentable over Furcht et al. (U.S. Patent No. 7,015,037, Provisional Priority to Aug. 5, 1999), in view of Crystal et al. (U.S. Patent Publication No: 2002/0076395; filed Dec., 23, 1998), and further in view of Baetge et al. (U.S. Patent No: 5.639.275; filed May 25, 1995); Claims 6-7 were rejected under 35 U.S.C. §103(a) as being unpatentable over Furcht et al. (U.S. Patent No. 7,015,037, Provisional Priority to Aug. 5, 1999), in view of Hertzel et al. (J. Lipid Res. 41:1082-1086; 2000); and Claims 6 and 19 were rejected under 35 U.S.C. §103(a) as being unpatentable over Furcht et al. (U.S. Patent No. 7,015,037, Provisional Priority to Aug. 5, 1999), in view of Hertzel et al. (J. Lipid Res. 41:1082-1086; 2000), and further in view of Zhang et al. (J. Endocrinology 164:119-128; 2000), in the previous office Action dated October 2, 2008. In view of the Declaration under 37 C.F.R. § 1.132 supplied by Mr. Masayuki Aso, and for reasons set forth above, the rejections are hereby withdrawn. Applicants' arguments are moot in view of the withdrawn rejections.

New Claim Rejections - 35 USC § 103

Claim 1-11, and 17-19 are newly rejected under 35 U.S.C. §103(a) as being unpatentable over Darimont et al. (WO 02/06450; Publication date: 24, January 2002), in view of Furcht et al. (U.S. Patent No. 7,015,037, Provisional Priority to Aug. 5, 1999).

The claims are directed to a population of primary cultured preadipocytes, wherein the preadipocytes stably maintain a foreign DNA encoding secreted insulin gene, operably linked to a promoter.

Darimont et al. describe the establishment of human preadipose cell lines capable of differentiating to adipose cells for development of drugs against obesity, diabetes and cardiovascular disease (Abstract). The isolation from subcutaneous adipose tissue and the

primary culture of preadipose cells by "ceiling culture method" is described on p. 7, Example 1, and p. 5, lines 20-29 and Fig. 1. The de-differentiation of adipocytes to preadipocytes is described in Example 2, p. 8. Darimont et al. further describe the immortalization of the cells by introducing and stably expressing the SV40 large T antigen via a retroviral vector (Example 3, p. 8).

While Darimont et al. do not describe the expression of a foreign insulin gene in the preadipocyte cell, such was known in the prior art. Furcht et al. teach multipotent adult stem cells that can be maintained in culture in the undifferentiated state, or differentiated to form cells of multiple tissue types, as well as methods for producing the same, for therapeutic use (Abstract). The isolation of the bone marrow derived mononuclear cells is described in Example 1(column 44), and their differentiation into adipocytes is outlined in Example 2 (column 46). The bone marrow derived stem cells are also referred to as mesenchymal stem cells and marrow stromal cells (column 49). Adipocytes derived from the stem cells can be used for the treatment of Type II diabetes (column 25). Furcht et al. describe a number of secreted genes that may be used for gene therapy of diabetes (column 30). Additionally described are viral transfer vectors, including retroviruses (column 32). Retroviral vectors are extensively described in column 35. Following *in vitro* culture and gene transfer, the transfected cells may be introduced locally or infused systemically (column 30). Specific examples of engraftment by intramuscular injection or stereotaxic transplantation into mice are described in Example 10 (columns 54-55). Furcht et al. describe the use of their adipocytes for implantation in reconstructive surgery, as well as treatment of Type II diabetes (column 25, lines 50-52), in addition to the encapsulation of genetically altered cells for delivery into a patient to produce insulin (paragraph 31, lines 35-64). Furcht et al. further teach that the genetically altered stem cells can also be encapsulated in an inert carrier to allow the cells to be protected from the host immune system while producing the secreted protein (column 31). A number of pharmaceutically acceptable inert carriers materials, that include polymers and capsules are described in column 31. The introduction of the cells into the body of a subject in conjunction with a suitable matrix implant or polymer capsule is described in column 8, lines 8-14). With specific reference to treatment for diabetes, the authors state that autologous stem cells that have been genetically altered with a retroviral vector to

produce insulin at physiologically therapeutic levels can be encapsulated for delivery within the patient's tissues, to produce insulin for extended periods of time (column 31). Furcht et al. further describe stem cells transfected with factor IX, that secrete the protein for at least 8 weeks after infusion into mice (column 30).

The inventions of both Darimont et al. and Furcht et al. are both directed to the transfection and differentiation of cells into adipocytes. Therefore, a person of ordinary skill in the art would have been motivated to combine their respective teachings and substitute primary cultured preadipocytes for stromal cell preadipocytes as a matter of design choice, and to forego the isolation and differentiation of stromal or mesenchymal stem cells. A person of ordinary skill in the art, having introduced an insulin gene by the expression vector of Furcht et al., to the primary cultured preadipocytes, of Darimont et al. would be able to practice the instantly claimed method of the invention, with a reasonable expectation of success. Thus it would have been *prima facie* obvious for a person of ordinary skill in the art, to introduce an insulin gene and an angiogenesis factor to preadipocytes, at the time of the instant invention.

Citation of Relevant Prior Art

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Kirkland et al. (U.S. Patent Application Publication 2005/0008621; effective filing date Oct. 6, 2001) disclose the isolation of primary preadipocyte cells from adipose or fat tissue and their subsequent culture, transfection and differentiation (paragraph [0045]; [0079]-[0084]).

Conclusion

Claims 1-11 and 17-19 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREYDOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Fereydoun G Sajjadi/
Primary Examiner, Art Unit 1633